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From: Hathaway Pease, Esq.
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Phone: (617) 227-7400
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Date: June 19, 2003

Pages: 10

(including cover page)

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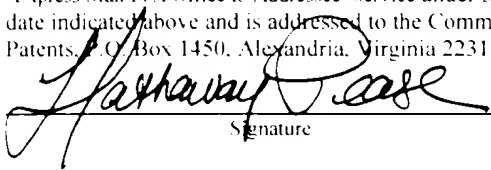
Re: U.S. Patent Application No.: 09/258600
For: *YEAST CELLS ENGINEERED TO PRODUCE PHEROMONE SYSTEM
PROTEIN SURROGATES AND USES THEREFOR*
Inventors: Fowlkes, Dana M. *et al.*
Filed: February 26, 1999
Our Ref. No.: CPI-012CP4DV

Dear Sir:

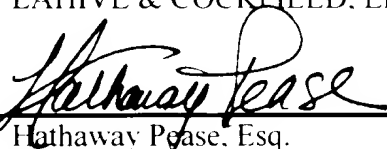
I enclose herewith for filing in the above-identified application the following:

1. Supplemental Information Disclosure Statement;
2. PTO Form 1449;
3. Copies of publications cited in PTO Form 1449 (140); and
4. A Return Postcard.

Please charge any necessary fees in connection with the enclosed statement to our Deposit Order Account No. 12-0080. For this purpose, a duplicate of this sheet is attached.

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Hathaway Pease, Esq., Reg. No. 46,488
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Respectfully submitted,
LAHIVE & COCKFIELD, LLP

Hathaway Pease, Esq.
Registration No. 46,488
Attorney for Applicants

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IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

In re the application of: Fowlkes, Dana M. *et al.*

Serial No.: 09/258600

Filed: February 26, 1999

For: *YEAST CELLS ENGINEERED TO PRODUCE
PHEROMONE SYSTEM PROTEIN SURROGATES
AND USES THEREFOR*

Attorney Docket No.: CPI-012CP4DV

Group Art Unit: 1636

Examiner: D. Lambertson

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SUPPLEMENTAL INFORMATION DISCLOSURE STATEMENT

Dear Sir:

Applicants and their Attorney are aware of the following additional publications, listed on the attached PTO Form 1449, and in accordance with 37 CFR §1.97 hereby submit these publications for the Examiner's consideration. A copy of each cited publication is enclosed.

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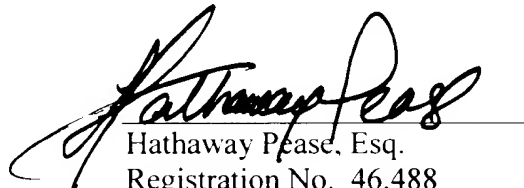
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Respectfully submitted,

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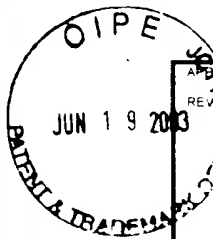


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LIST OF PUBLICATIONS CITED BY APPLICANT (Use several sheets if necessary)				
APPLICANT Fowlkes, Dana M. et al.			FILING DATE February 26, 1999	
			GROUP 1636	

OTHERS (including Author, Title, Date, Pertinent Pages, Etc.)

B1	Akada, R. et al. "Genetic Relationships Between the G Protein $\beta\gamma$ Complex, Ste5p, Ste20p and Cdc42p: Investigation of Effector Roles in the Yeast Pheromone Response Pathway," <i>Genetics</i> 143:103-117 (1996).
B2	Alison, Malcolm R. et al. "Growth factors and growth factor receptors," <i>Brit. J. of Hosp. Med.</i> 49(11):774-88 (1993).
B3	Altieri, Dario C. "Proteases and protease receptors in modulation of leukocyte effector functions," <i>J. of Leukocyte Biol.</i> 58:120-27 (1995).
B4	Artemyev, Nikolai O. et al. "Sites of Interaction between Rod G-Protein α -Subunit and cGMP-phosphodiesterase γ -Subunit," <i>J. Biol. Chem.</i> 267(35):25067-72 (1992).
B5	Belka, C. et al. "The role of tyrosine kinases and their substrates in signal transmission of hematopoietic growth factors: a short review," <i>Leukemia</i> 9:754-61 (1995).
B6	Bender, Alan and Sprague, George F. Jr. "Pheromones and Pheromone Receptors Are the Primary Determinants of Mating Specificity in the Yeast <i>Saccharomyces cerevisiae</i> ," <i>Genetics</i> 121:463-76 (1989).
B7	Birnbaumer, Lutz "Transduction of receptor signal into modulation of effector activity by G proteins: the first 20 years or so . . ." <i>FASEB Journal</i> 4:3178-88 (1990).
B8	Blinder, Dmitry et al. "Constitutive Mutants in the Yeast Pheromone Response: Ordered function of the Gene Products," <i>Cell</i> 56:479-486 (1989).
B9	Bray, P. et al., "Human cDNA clones for four species of $G_{\alpha s}$ signal transduction protein," <i>PNAS USA</i> , 83(23):8893-7 (1986).
B10	Bray, P. et al., "Human cDNA clones for an α subunit of G_i signal-transduction protein," <i>PNAS USA</i> , 84(15):5115-19 (1987).
B11	Brill, Julie A. et al. "A Role for Autophosphorylation Revealed by Activated Alleles of <i>FUS3</i> , the Yeast MAP Kinase Homolog," <i>Molecular Biology of the Cell</i> 5:297-312 (1994).
B12	Brugarolas, James et al. "Radiation-induced cell cycle arrest compromised by p21 deficiency," <i>Nature</i> 377:522-57 (1995).
B13	Burack, W. Richard et al. "The Activating Dual Phosphorylation of MAPK by MEK Is Nonprocessive," <i>Biochemistry</i> 36(20):5929-5933 (1997).
B14	Cavallini, Bruno et al. "A yeast activity can substitute for the HeLa Cell TATA box factor," <i>Nature</i> 334:77-80 (1988).
B15	Chambers, D. A. et al. "Neuroimmune Modulation: Signal Transduction and Catecholamines," <i>Neurochem. Int.</i> 22(2):95-110 (1993).
B16	Chan, Russell K. and Otte, Carol A. "Isolation and Genetic Analysis of <i>Saccharomyces cerevisiae</i> Mutants Supersensitive to G1 Arrest by a Factor and α Factor Pheromones," <i>Molecular and Cellular Biol.</i> 2(1) 11-20 (1982).
B17	Chang, Fred and Herskowitz, Ira "Identification of a Gene Necessary for Cell Cycle Arrest by a Negative Growth Factor of Yeast: FAR1 is an Inhibitor of a G1 Cyclin, CLN2," <i>Cell</i> 63:999-1011 (1990).
B18	Clark, Karen L. et al. "Interactions among the Subunits of the G protein Involved in <i>Saccharomyces cerevisiae</i> Mating," <i>Molecular and Cellular Biol.</i> 13(1):1-8 (1993).
B19	Cole, Gary M. et al. "Stoichiometry of G Protein Subunits Affects the <i>Saccharomyces cerevisiae</i> Mating Pheromone Signal Transduction Pathway," <i>Molecular and Cellular Biology</i> 10(2):510-517 (1990).

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LIST OF PUBLICATIONS CITED BY APPLICANT (Use several sheets if necessary)		APPLICANT Fowlkes, Dana M. et al.	GROUP 1636
		FILING DATE February 26, 1999	TECH CENTER 1600/2800 JUN 24 2003

OTHERS (including Author, Title, Date, Pertinent Pages, Etc.)

	C1	Coleman, David E. et al. "Structures of Active Conformation of G _{α1} and the Mechanism of GTP Hydrolysis," <i>Science</i> 265:1405-12 (1994).
	C2	Conklin, Bruce R. et al. "Substitution of three amino acids switches receptor specificity of G _α to that of G _α ," <i>Nature</i> 363:274-76 (1993).
	C3	Dietzel, Christine et al. "Pheromonal regulation and sequence of the <i>Saccharomyces cerevisiae</i> SST2 gene: a model for desensitization to pheromone." <i>Mol. Cell. Biol.</i> 7(12):4169-4177, Dec. 1987.
	C4	Dietzel, Christine and Kurjan, Janet "The Yeast SCG1 Gene: A G _α -like Protein Implicated in the a- and α-Factor Response Pathway," <i>Cell</i> 50:1001-10 (1987).
	C5	Dmochowska, Aleksandra et al. "Yeast KEX1 Gene Encodes a Putative Protease with a Carboxypeptidase B-like Function Involved in Killer Toxin and α-Factor Precursor Processing," <i>Cell</i> 50:573-84 (1987).
	C6	Dolan, J. W. et al. "Overproduction of the yeast STE12 protein leads to constitutive transcriptional induction," <i>Genes & Development</i> 4(4):492-502 (1990).
	C7	Dubois, Patrice M. et al. "Role of the transmembrane and cytoplasmic domains of surface IgM in endocytosis and signal transduction," <i>Eur. J. Immunol.</i> 22:851-57 (1992).
	C8	Erickson, Deborah "Intercepted Messages: New biotechnology drugs target intracellular communication," <i>Scientific American</i> 267(5):122-23 (1992).
	C9	Etienne, Gilles et al. "A Screening Method for Antifungal Substances Using <i>Saccharomyces cerevisiae</i> Strains Resistant to Polyene Macrolides," <i>J. of Antibiotics</i> 43(2):199-206 (1990).
	C10	Fasullo, Michael T. and Davis, Ronald W. "Direction of Chromosome Rearrangements in <i>Saccharomyces cerevisiae</i> by Use of <i>his3</i> Recombinational Substrates," <i>Molecular and Cellular Biol.</i> 8(10):4370-80 (1988).
	C11	Ferrell, James E. Jr. "Tripping the switch fantastic: how a protein kinase cascade can convert graded inputs into switch-like outputs," <i>Trends in Biochem. Sci.</i> 21(12):460-6 (1996).
	C12	Ferrell, James E. Jr. et al. "The Biochemical Basis of an All-or-None Cell Fate Switch in <i>Xenopus</i> Oocytes," <i>Science</i> 280:895-898 (1998).
	C13	Franke, Arthur E. et al. "Human C5a Anaphylatoxin: Gene Synthesis, Expression, and Recovery of Biologically Active Material from <i>Escherichia coli</i> ," <i>Methods in Enzymology</i> 162:653-68 (1988).
	C14	Funaro, Ada et al. "Human CD38 is associated to distinct molecules which mediate transmembrane signaling in different lineages," <i>Eur. J. Immunol.</i> 23:2407-11 (1993).
	C15	Gallego, Carme, et al. "Myristoylation of the G _{α2} polypeptide, a G protein α subunit, is required for its signaling and transformation functions," <i>Proc. Natl. Acad. Sci. USA</i> 89:9695-99 (1992).
	C16	Garritsen, Anja et al. "The N-Terminal coiled-coil domain of β is essential for γ association: A Model for G-Protein βγ subunit interaction," <i>Proc. Natl. Acad. Sci. USA</i> 90:7706-10 (1993).
	C17	Gerard, Norma P. and Gerard, Craig "Construction and Expression of a Novel Recombinant Anaphylatoxin, C5a-N19, a Probe for the Human C5a Receptor," <i>Biochemistry</i> 29(39):9274-81 (1990).
	C18	Gordon, J. "B-cell signaling via the C-type lectins CD23 and CD72," <i>Immunology Today</i> 15(9):411-17 (1994).

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		FILING DATE February 26, 1999	

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OTHERS (including Author, Title, Date, Pertinent Pages, Etc.)

D1	Graf, Rolf <i>et al.</i> "A Truncated Recombinant α Subunit of G_{13} with a Reduced Affinity for $\beta\gamma$ Dimers and Altered Guanosine 5'-3-O-(Thio)triphosphate Binding," <i>J. of Biol. Chem.</i> 267(34):24307-14 (1992).
D2	Gros, Philippe <i>et al.</i> "Mammalian Multidrug Resistance Gene: Complete cDNA Sequence Indicates Strong Homology to Bacterial Transport Proteins," <i>Cell</i> 47:371-80 (1986).
D3	Hagen, David C. <i>et al.</i> "Evidence the yeast <i>STE3</i> gene encodes a receptor for the peptide pheromone a factor: Gene sequence and implications for the structure of the presumed receptor," <i>Proc. Natl. Acad. Sci. USA</i> 83:1418-22 (1986).
D4	Hall, Marcia <i>et al.</i> "Evidence for different modes of action of cyclin-dependent kinase inhibitors: p15 and p16 bind to kinases, p21 and p27 bind to cyclins," <i>Oncogene</i> 11:1581-88 (1995).
D5	Harbury, Pehr B. <i>et al.</i> "A Switch Between Two-, Three- and Four-Stranded Coiled Coils in GCN4 Leucine Zipper Mutants," <i>Science</i> 262:1401-07 (1993).
D6	Hartwell, Leland H. "Mutants of <i>Saccharomyces cerevisiae</i> Unresponsive to Cell Division Control by Polypeptide Mating Hormone," <i>J. Cell Biol.</i> 85:811-22 (1980).
D7	Hasson, M.S. <i>et al.</i> "Mutational Activation of the <i>STE5</i> Gene Product Bypasses the Requirement for G Protein β and γ Subunits in the Yeast Pheromone Response Pathway," <i>Molecular and Cellular Biology</i> 14(2):1054-1065 (1994).
D8	He, Bin <i>et al.</i> " <i>RAM2</i> , an essential gene of yeast, and <i>RAM1</i> encode the two polypeptide components of the farnesyltransferase that prenylates a-actor and Ras proteins," <i>Proc. Natl. Acad. Sci. USA</i> 88:11373-77 (1991).
D9	Hiltunen, J. Kalervo <i>et al.</i> "Peroxisomal Multifunctional β -Oxidation Protein of <i>Saccharomyces cerevisiae</i> ," <i>J. of Biol. Chem.</i> 267(10):6646-6653 (1992).
D10	Hrycyna, Christine A. <i>et al.</i> "The <i>Saccharomyces cerevisiae STE14</i> gene encodes a methyltransferase that mediates C-terminal methylation of a-factor and RAS Proteins," <i>The EMBO J.</i> 10(7):1699-1709 (1991).
D11	Huang, Chi-Ying F. <i>et al.</i> "Ultrasensitivity in the mitogen-activated protein kinase cascade," <i>Proc. Natl. Acad. Sci. USA</i> 93:10078-10083 (1996).
D12	Imamoto, Akira <i>et al.</i> "Genetics of signal transduction: tales from the mouse," <i>Curr. Opin. Gen. & Dev.</i> 4:40-46 (1994).
D13	Inouye, Carla <i>et al.</i> "Ste5 RING-H2 Domain: Role in Ste4-Promoted Oligomerization for Yeast Pheromone Signaling," <i>Science</i> 278:103-106 (1997).
D14	Jabbar, M. Abdul <i>et al.</i> "Influenza Viral (A/WSN/33) hemagglutinin is expressed and glycosylated in the yeast <i>Saccharomyces cerevisiae</i> ," <i>Proc. Natl. Acad. Sci. USA</i> 82:2019-23 (1985).
D15	Jakobs, K. H. <i>et al.</i> "Dual regulation of adenylate cyclase. A signal transduction mechanism of membrane receptors," <i>Basic Res. Cardiol.</i> 81:1-9 (1986).
D16	Journot, Laurent <i>et al.</i> "Amino Acids 367-376 of the G_s α subunit induce membrane association when fused to soluble amino-terminal deleted G_{11} α subunit," <i>Proc. Natl. Acad. Sci. USA</i> 88:10054-58 (1991).
D17	Julius, David <i>et al.</i> "Glycosylation and Processing of Prepro- α -Factor through the Yeast Secretory Pathway," <i>Cell</i> 36:309-18 (1984).
D18	Julius, David <i>et al.</i> "Isolation of the Putative Structural Gene for the Lysine-Arginine-Cleaving Endopeptidase Required for Processing of Yeast Prepro- α -factor," <i>Cell</i> 37:1075-89 (1984).
D19	Julius, David <i>et al.</i> "Yeast α Factor is Processed from a Larger Precursor Polypeptide: The Essential Role of a Membrane-Bound Dipeptidyl Aminopeptidase," <i>Cell</i> 32:839-52 (1983).

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E1	Kaiser, Chris A. et al. "Many Random Sequences Functionally Replace the Secretion Signal Sequence of Yeast Invertase," <i>Science</i> 235:312-17 (1987).
E2	Kingsman, S.M. et al. "The production of mammalian protein in <i>Saccharomyces cerevisiae</i> ," <i>Tibtech</i> 5:53-57 (1987).
E3	Kosugi, Shinji et al. "Characterization of heterogeneous mutations causing constitutive activation of the luteinizing hormone receptor in familial male precocious puberty," <i>Human Molecular Genetics</i> 4(2):183-88 (1995).
E4	Kramer, R. A. et al. "HTLV-III gag Protein Is Processed in Yeast Cells by the Virus pol-Protease," <i>Science</i> 231:1580-85 (1986).
E5	Kuchler, Karl and Thorner, Jeremy "Functional expression of human <i>mdr1</i> in the yeast <i>Saccharomyces cerevisiae</i> ," <i>Proc. Natl. Acad. Sci. USA</i> 89:2302-06 (1992).
E6	Kuchler, Karl et al. " <i>Saccharomyces cerevisiae</i> STE6 gene product: a novel pathway for protein export in eukaryotic cells," <i>The EMBO J.</i> 8(13):3973-84 (1989).
E7	Kurjan, Janet " α -Factor Structural Gene Mutations in <i>Saccharomyces cerevisiae</i> : Effects on α -Factor Production and Mating," <i>Molecular and Cellular Biol.</i> 5(4):787-96 (1985).
E8	Kurjan, Janet and Herskowitz, I. "Structure of a Yeast Pheromone Gene (<i>MFα</i>): A Putative α -Factor Precursor Contains Four Random Copies of Mature α -Factor," <i>Cell</i> 30:933-43 (1982).
E9	Lambright, David G. et al. "Structural determinants for activation of the α -subunit of a heterotrimeric G protein," <i>Nature</i> 369:621-28 (1994).
E10	Leberer, Ekkehard et al. "Dominant-negative mutants of a yeast G-protein β subunit identify two functional regions involved in pheromone signalling," <i>The EMBO J.</i> 11(13):4805-13 (1992).
E11	Lee, Ethan et al. "The G226A Mutant G β Highlights the Requirement for Dissociation of G Protein Subunits," <i>J. Biol. Chem.</i> 267(2):1212-18 (1992).
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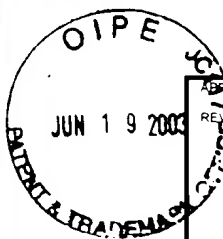
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ATTY DOCKET NO.

SERIAL NO.

CPI-012CP4DV

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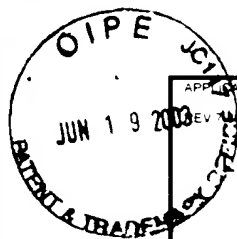
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